PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference ITR0073Y	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/EP2005/001114	International filing date *(day/month/year)* 03 February 2005 (03.02.2005)	Priority date *(day/month/year)* 11 February 2004 (11.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P ANGELETTI SPA		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 14 August 2006 (14.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Ellen Moyse e-mail: pt05@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/001114	03.02.2005	11.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07K14/705, C12N15/62, A61K39/00, A61P35/00

Applicant
ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-5,9,10,14-23,29-32 (all partially), 6,24-28,33-35 (all complete)

because:

☒ the said international application, or the said claims Nos. 24-28,33-35 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-5,9,10,14-23,29-32 (all partially), 6 (complete)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-5,9,10,14-35 (all partially), 7,8,11-13 (all complete)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3, 7, 8, 11-13 (complete), 1, 2, 4, 5, 10, 14-23, 29-32 (all partially)
	No:	Claims	1,2,4,5,9,10,14,15,20,32 (all partially)
Inventive step (IS)	Yes:	Claims	3, 7, 8, 11-13 (complete), 1, 2, 4, 5, 10, 14-23, 29-32 (all partially)
	No:	Claims	16-19,21-23,29-31 (all partially)
Industrial applicability (IA)	Yes:	Claims	1-5,7-23,29-32
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

   see form 210

Additional remark to item I

The application encloses a sequence listing (pages 1-48) not integrated into the description.

Additional remark to item III

The international search report has been drawn up in respect to only part of the claims of the international application as filed. Since only claims searched will be the subject of the international preliminary examination (Rule 66.1(e) PCT) and since claims 24-28, 33-35 are directed to a method of treatment of the human/animal body which will not require an international preliminary examination (Rule 67.1(iv) PCT), this written opinion is solely based on claims 1-5, 9, 10, 14-23 and 29-32 (all partially) and claims 7, 8, 11-13 (all complete), i.e. inventions 1 and 5 of the international application as indicated below unter item IV.

Additional remark to item IV

This Authority considers that there are 5 inventions covered by the claims indicated as follows:

1) CEA-DOM fusion, nucleic acid, protein, vector, host cell, method of production and use in vaccine against cancer
2) CEA-FcIgG fusion, nucleic acid, protein, vector, host cell, method of production and use in vaccine against cancer
3) CEA-CT fusion, nucleic acid, protein, vector, host cell, method of production and use in vaccine against cancer
4) CEA-LTA fusion, nucleic acid, protein, vector, host cell, method of production and use in vaccine against cancer
5) CEA-LTB fusion, nucleic acid, protein, vector, host cell, method of production and use in vaccine against cancer

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The application is based on different carcinoembryonic antigen (CEA) fusion proteins, their production and use. The technical relationship and thus common concept within the meaning of Rule 13.2 PCT a priori linking such fusion proteins is considered to be based on that CEA is part of the fusion protein and that the fusion protein is capable of producing an immune response in a mammal. The prior art, however, already discloses this common concept, e.g. Rice J et al (2001), J. Immunol. 167:1558-1565 (D1) which comprises p.DOM-CEA used in DNA vaccination of mice and Lund L et al (2003), Cancer Gene Therapy 10(5):365-376 (D2) enclosing CEA-tetanus toxoid fusion in DNA-vaccination. Thus there is no single inventive concept (Rule 13.1 PCT) underlying a unique invention and consequently there is lack of unity.

Additional remarks to item V

1. The subject-matter of claims 1-5,7-9,13-22 and 29-32 is not clearly defined in that it refers to nucleic acids or polypeptides. Nucleic acids and polypeptides are chemical compounds and as such have to be defined by structural features, i.e. their sequence (Article 6 PCT).

2. Reference is made to the following documents:

D1: RICE J ET AL: "DNA fusion vaccine designed to induce cytotoxic T cell responses against defined peptide motifs: implications for cancer vaccines." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 1 AUG 2001, vol. 167, no. 3, 1 August 2001 (2001-08-01), pages 1558-1565, XP002326986 ISSN: 0022-1767

D2: LUND LARS H ET AL: "Signal sequence deletion and fusion to tetanus toxoid epitope augment antitumor immune responses to a human carcinoembryonic antigen (CEA) plasmid DNA vaccine in a murine test system." CANCER GENE THERAPY. MAY 2003, vol. 10, no. 5, May 2003 (2003-05), pages 365-376, XP002326987 ISSN: 0929-1903

D3: WO 03/059379 A (PHARMEXA A/S; KLYSNER, STEEN; VOLDBORG, BJOERN) 24 July 2003 (2003-07-24)

D4: US-B1-6 482 614 (YOUNG RICHARD A) 19 November 2002 (2002-11-19)

D5: WO 01/30382 A (AVENTIS PASTEUR LIMITED; BERINSTEIN, NEIL;

TARTAGLIA, JAMES; MOINGEON,) 3 May 2001 (2001-05-03)

3. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1,2,4,5,9,10,14,15,20 and 32 is not new in the sense of Article 33(2) PCT with regard to invention 1 (CEA-DOM fusion):

   Document D1 discloses DNA fusion vaccine consisting of CEA fused to DOM (p.DOM-CEA) and its implication for cancer treatment.

4. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 16-19,21-23 and 29-31 does not involve an inventive step in the sense of Article 33(3) PCT with regard to invention 1 (CEA-DOM fusion):

   The production of a protein from a given DNA sequence as well as the selection of an alternative vector well known to the skilled person, is considered as the outcome of routine experimentation that does not involve inventive skill.

5. The present application meets the criteria of Article 33(1) PCT with regard to invention 5 (CEA-LTB fusion) since the prior art neither teaches nor suggests the preparation and use of CEA-LTB fusion proteins for producing an immune response in a mammal.